

**Standardized Postmortem Examination Guidelines for Individuals Dying After
Environmental Exposures Related to the Collapse of the World Trade Center on
September 11, 2001**

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1 **Introduction**

2 Destruction of the World Trade Center (WTC) on September 11, 2001 caused the
3 largest acute environmental disaster in the history of New York City (Claudio 2001;
4 Landrigan 2001; Landrigan et al. 2004; Nordgren et al. 2002).

5 The National Resources Defense Council and others determined in 2002 that a
6 comprehensive health registry of individuals exposed to air contaminants in the aftermath
7 of the destruction of the WTC on September 11 was needed to assess the potential health
8 impacts and consequences over time of the high intensity environmental pollution that
9 resulted. Several such programs are currently in place, including the Mount Sinai World
10 Trade Center Medical Monitoring Program (Herbert et al. 2006), the Fire Department of
11 New York (FDNY) WTC Medical Monitoring and Treatment Program, and the
12 collaborative World Trade Center Health Registry hosted by the New York City
13 Department of Health and Mental Hygiene (NYC DOHMH) and supported by
14 ATSDR/CDC (Brackbill et al. 2006; link to registry found at: www.wtcregistry.org).

15 These programs have provided important data that has informed development of clinical
16 guidelines to identify, evaluate, treat, and refer patients with conditions that could be
17 related to the WTC disaster (Friedman et al. 2006; accessible at
18 <http://www.nyc.gov/html/doh/downloads/pdf/chi/chi25-7.pdf>).

19 Although much has been learned about the health problems experienced by
20 exposed individuals in the five years since the WTC collapse, many questions remain
21 about both current health problems and health effects that exposed people may yet
22 develop over the long term. In particular, there has been great public concern that deaths
23 of exposed individuals caused by conditions such as cancer may have been related to

1 their exposures. Unequivocal documentation of associations between such conditions
2 and the WTC collapse will require epidemiological evaluations of populations, and it will
3 be years before definitive studies can be performed. In the meantime, there is a current
4 and pressing need for guidance in the approach to individual cases that may be related to
5 exposures associated with the WTC collapse. The need is further exacerbated by the
6 planned implementation of a new WTC fatality investigations program that may evaluate
7 many such cases.

8 These guidelines have been developed in response to the need for a standardized
9 approach to postmortem examination of individuals exposed to the WTC disaster.

10 Because individuals who were exposed to the WTC disaster can be found across the
11 country, consistent standards are a need not only for New York, but for the entire nation.

12 These guidelines are intended not only to potentially benefit families of individual
13 decedents, but also to provide pathological data that will help clinicians to better
14 understand and treat the conditions affecting survivors of the WTC collapse.

15 Recommendations such as those for collection and retention of tissues may also facilitate
16 scientific research to better understand exposures and health effects caused by the WTC
17 collapse.

18 **Exposures after the WTC Attacks**

19 The combustion of jet fuel at temperatures above 1000°C resulted in a dense and
20 toxic atmospheric plume containing a complex mixture of materials including soot,
21 metals, volatile organic compounds, and acid gases. The eventual collapse of the World
22 Trade Center towers pulverized concrete, glass, and other building contents, generating
23 tons of particulate matter composed of concrete dust, fiberglass, asbestos, lead,

1 polychlorinated biphenyls, organochlorine pesticides, and polychlorinated furans and
2 dioxins, which dispersed over lower Manhattan and beyond. Exposures continued long
3 after September 11th due to disturbance of settled dust and persisting fires at the WTC site
4 (Landrigan et al. 2004; McGee et al. 2003; Nordgren et al. 2002; Liroy et al. 2002).

5 **Overview of medical conditions associated with the WTC collapse**

6 In the five years since the WTC attacks, a number of health effects related to
7 WTC exposures have been documented. From early after the collapse, clinical and
8 epidemiological assessments have documented a high prevalence of respiratory
9 symptoms in exposed individuals (CDC 2002; Landrigan et al. 2004; Brackbill et al.
10 2006; Herbert et al. 2006). Persistent cough, reactive airways dysfunction syndrome,
11 asthma, and chronic obstructive pulmonary disease have been reported in some workers
12 involved in the aftermath of the WTC collapse (Prezant et al. 2002; Skloot et al., 2004).
13 Symptoms of gastroesophageal reflux have been an unexpected but common problem in
14 exposed people (Prezant et al. 2002). Rare reports have included granulomatous
15 pneumonitis related to foreign body deposition (Safirstein et al. 2003) and eosinophilic
16 pneumonitis (Rom et al. 2002).

17 It is unclear what long-latency conditions will develop over time. Given the range
18 of environmental hazards produced by the WTC collapse, the range of individual
19 exposures, and the varied susceptibilities of exposed individuals, a broad range of
20 illnesses and pathologies may occur among exposed individuals over time. Concerns
21 have already been expressed that conditions such as cancer and sarcoidosis may have
22 resulted from WTC exposures. Clearly, there is a need for organized follow-up of deaths
23 of people exposed to the WTC collapse.

Autopsy protocol

This protocol describes the recommended techniques for postmortem examination of an individual who is suspected to have died at least in part due to exposure to the collapse of the WTC. It is not intended to replace standard autopsy technique but, rather, provide additional guidance for hospital pathologists, forensic pathologists, and others involved in postmortem examination of such individuals described herein. In light of the potential for inhalational-type injury, careful attention to examination of the upper and lower respiratory tracts and upper gastrointestinal tract is warranted. As it has done in the past with other diseases, the autopsy may make significant contributions to our understanding of diseases related to exposures associated with the WTC collapse by elucidating specific pathologic entities or identifying potential markers of exposure. The actual performance of the autopsy dissection should be considered only a part of the postmortem examination as a whole, which also relies heavily on vigorous clinical review and correlation with pathologic findings. Such clinical reviews will, likely, require communication with programs currently in place to track exposed individuals and document their exposures, including the Mount Sinai World Trade Center Medical Monitoring Program, the FDNY WTC Medical Monitoring and Treatment Program, and the World Trade Center Health Registry.

Clinical Information

Both clinical and pathological information must be considered in evaluating a decedent's cause of death and contributing conditions. For diffuse lung diseases, especially the interstitial lung diseases, a multi-disciplinary approach using clinical, radiological, and pathological information is often required for optimal interpretation and

1 meaningful diagnosis. Appropriate medical record reviews and witness interviews
2 should be performed. Clinical guidelines have been developed to aid in obtaining
3 appropriate exposure and symptom histories, which are very important to consider in
4 assessment of causation (Friedman et al. 2006; accessible at
5 <http://www.nyc.gov/html/doh/downloads/pdf/chi/chi25-7.pdf>). History should include
6 inquiries about the following:

- 7 • Direct exposure to the cloud of debris and dust released by the collapse of the
8 towers;
- 9 • Duration, type, and intensity of exposure to dust, smoke, and fumes in the days
10 and months after the disaster; and
- 11 • Whether onset of symptoms occurred after, but within plausible proximity to,
12 WTC exposure.

13 In addition to history of WTC-related exposures, other relevant occupational and
14 environmental history should be obtained. Smoking status, recreational activities, and
15 social history are also important. Documentation should also be sought about how long
16 medical conditions of concern have been present.

17 **General Approach**

18 A complete postmortem examination should take place as soon as possible after
19 death, using any of a number of standard general and specific autopsy techniques. A
20 narrative description of such standard autopsy techniques is beyond the scope of these
21 guidelines and the reader is referred to standard references of autopsy technique (Ludwig
22 2002; Hutchins et al. 1994). Although complete postmortem examination is preferred,
23 limited autopsy (especially in hospital-based cases) may be preferred by some next-of-

1 kin. In such instances, the importance of examination of the upper and lower respiratory
2 tracts and upper gastrointestinal tract, in addition to clinically suggested areas, should be
3 stressed to next-of-kin granting permission.

4 **Tissue Sampling and Histological Examination**

5 In light of the high potential for respiratory-based illness, particular attention
6 should be focused on evaluation of the upper and lower respiratory tracts.

7 Formalin perfusion fixation, using methods previously described (Ludwig 2002)
8 is the preferred method for fixation and evaluation of the lungs. For all cases, a minimum
9 of two sections per lobe from both lungs, sections of upper and lower airways, and
10 sections of visceral and parietal pleura should be submitted for histologic examination
11 using standard hematoxylin and eosin (H&E) staining techniques. In cases of known or
12 suspected fibrosing lung disease, special care should be made **not** to focus tissue
13 sampling solely on fibrotic areas of the affected lung(s) but to adequately sample
14 "normal" areas or "less affected" areas adjacent to fibrotic areas of the lung. Similarly, if
15 lung cancer is present, both the tumor and uninvolved areas of lung should be sampled.
16 If lung cancer or mesothelioma is present, a minimum of two tissue blocks should be
17 taken from involved areas.

18 While light microscopic evaluation of standard H&E-stained sections of lung
19 using polarizing lenses and/or special histochemical stains (i.e., iron stains for
20 ferruginous bodies) can provide useful semi-quantitative information about particulate
21 matter in the lungs, the circumstances of the WTC collapse require a more quantitative
22 mineralogical assessment of tissues. Methods, such as atomic absorption spectrometry
23 (AAS) and energy-dispersive X-ray spectroscopy (EDS), can help further elucidate the

1 type of particulate matter to which an individual may have been exposed. Testing should
2 be performed by an experienced laboratory with appropriate quality assurance controls.
3 Over time, clearance mechanisms will likely result in reduced measured tissue burdens,
4 which should not be misinterpreted as indicating a level of exposure lower than the
5 individual's actual exposure at the time of the WTC disaster.

6 Tissue samples from each lung should also be fixed in glutaraldehyde for further
7 studies via electron microscopy (see below under special studies for further instructions).

8 A minimum of 50 g of lung tissue from each lung should be fixed in 10%
9 formalin and another 50 g snap-frozen in liquid nitrogen and then maintained frozen at -
10 80 °C (or, if snap-freezing is not possible, simply frozen at -80 °C) and kept for
11 additional studies as outlined below. Such tissues will be maintained for further studies if
12 needed.

13 If mineral fiber analysis is contemplated, European guidelines recommend
14 pooling 3 lung pieces of 1-2 cm³, one from the apex of the upper lobe, one from the apex
15 of the lower lobe, and one from the base of the lower lobe. Tumor tissue should be
16 avoided, because it contains few particles and can result in a false-negative fiber count.
17 Paraffin wax can be contaminated by asbestos fibers, so paraffin embedding should be
18 avoided (De Vuyst et al. 1998). Sample drying and traumatic manipulations should be
19 avoided, because they can cause fiber breakage and affect determination of fiber length
20 (Dodson 2006).

21 Additional tissues that should be evaluated by standard H&E-stained sections
22 include:

- 23 • Brain

- 1 • Upper, middle, and lower esophagus (GE junction)
- 2 • Heart (sections of ventricular myocardium and coronary vessels)
- 3 • Lymph nodes (preferably thoracic/ mediastinal and abdominal/ mesenteric)
- 4 • Liver
- 5 • Pancreas
- 6 • Spleen
- 7 • Stomach
- 8 • Small and large intestine
- 9 • Kidney
- 10 • Adrenal
- 11 • Vertebral bone marrow
- 12 • Other organs as guided by macroscopic findings and/or clinical records

13 **Toxicology**

14 Ideally, certain body fluids and tissue samples should be retained for possible
15 toxicological studies:

- 16 • Blood: Antemortem blood should be spun down and the supernatant saved
17 (frozen) for potential future studies. If antemortem blood is not available,
18 postmortem blood from "central" acquisition (i.e., heart) or "peripheral"
19 acquisition (i.e., femoral puncture) can be saved in a similar fashion.
- 20 • Urine: Urines samples should be saved (frozen) for potential future
21 evaluation for toxins of concern.
- 22 • Solid organs: Liver is the solid organ of choice if liquid specimens (i.e.,
23 blood) are not available. If blood is not available, a fresh sample of 50-100 g of

1 liver tissue from the right lobe can be frozen for potential future toxicological
2 studies.

3 **Special studies**

4 Electron Microscopy (EM): Specimens can be sent to and evaluated by a
5 designated facility utilizing EM to assess the presence of particulate metals, minerals
6 (including asbestos fibers and other silicates [i.e., quartz]), and fibrous glass.

7 Specimens should be fixed in an appropriate aldehyde (3% glutaraldehyde)
8 solution. Ideally, the specimen should be cut into cubes of less than 3 mm square and
9 placed in fixative as quickly as possible. Tissues to be evaluated by EM should not
10 remain in fixative for more than 4 days. Specimens should be referred for evaluation
11 before then or, if longer term storage is anticipated before referral, the tissue should be
12 embedded in plastic according to standard preparation of samples for EM study.

13 Alternatively, formalin-fixed and paraffin-embedded tissues or formalin-fixed
14 tissues alone may be submitted for evaluation by EM (although contamination of paraffin
15 by asbestos fibers is a potential concern for mineral fiber analyses).

16 Mineralogical evaluation: Specimens can be further evaluated at a designated
17 facility by additional studies (i.e., EDS and AAS) designed to identify and quantify
18 elemental composition of particles in tissues. Glutaraldehyde-fixed tissues are preferable
19 for evaluation by EDS, though formalin-fixed tissues may be used.

20 Controls for EM and Mineralogical Analyses: Because mineral particles and
21 fibers can be detected in the lungs of anyone if highly sensitive methods are used,
22 interpreting measured lung burden of particles and fibers requires a control population
23 and reference values for the methods used. Variables such as age, sex, smoking,

1 occupational exposures, and rural vs. urban residence should all be considered in defining
2 control populations to establish reference values (De Vuyst et al. 1998).

3 Access to Stored Tissues and Body Fluids: Formalin-fixed and/or frozen tissues
4 or body fluids preserved according to these guidelines should be stored in a fashion that
5 facilitates access for future study, such as at a designated facility. Appropriate local
6 oversight and procedures will need to be developed to track inventory and manage access
7 to stored samples in the event of specific findings that warrant further study or the
8 development of novel approaches for evaluation of stored samples.

9 **Assessment of Information and Categorization of Relation to WTC Exposures**

10 The basic approach to evaluation of autopsy information in the setting of WTC
11 exposures is much the same as in other autopsy settings. Gross and histological findings
12 of disease, mineral and mineral fiber analyses, and clinical information should be
13 correlated, leading to determination of the disease causing death and concurrent
14 pathologic processes. In addition to describing and diagnosing disease manifestations,
15 correlation of pathological and clinical information also underlies determination of extent
16 and severity of disease, an important issue in compensation settings.

17 A unique feature of determining cause of death in those with histories of
18 environmental exposures related to the WTC collapse is the desire on the part of
19 decedents' families and loved ones to know if WTC exposures caused the diseases
20 leading to death. As already noted, at this point in time, in many (perhaps most) cases
21 there will likely be insufficient data to definitively address this question due to the lack of
22 sufficient case reports and epidemiological data documenting associations between
23 exposures and mortality.

1 The issue of how causality between WTC-related exposures and adverse health
2 effects will be established and categorized over time is an important one. An Institute of
3 Medicine report issued in 1994 provides relevant guidance on assessing causal links
4 between exposures and adverse health effects (IOM 1994). The report also provides a
5 system for categorizing the level of certainty that an implicated exposure is causal.
6 Although that report focused on adverse reactions to pediatric immunizations, the
7 approach it took to assessing causality is very relevant to the issue of determining
8 causation of adverse health effects by WTC-related exposures. In the current setting of
9 scientific uncertainty, use of the following categories and descriptions adapted from the
10 IOM report is recommended to classify the relationship between death and WTC
11 exposure [italicized text excerpted directly from the Institute of Medicine report (IOM
12 1994)]:

13 Level 1: *The evidence establishes a causal relation: Epidemiologic studies and/or*
14 *case reports provide unequivocal evidence for a causal relation, and biologic plausibility*
15 *has been demonstrated.*

16 Level 2: *The evidence favors acceptance of a causal relation: The balance of*
17 *evidence from one or more case reports or epidemiologic studies provides evidence for a*
18 *causal relation that outweighs the evidence against such a relation. Demonstrated*
19 *biologic plausibility...is... supportive of a decision to accept a causal relation but*
20 *insufficient on its own....*

21 Level 3: *The evidence favors rejection of a causal relation: Only evidence from*
22 *epidemiologic studies...should be...a basis for possible rejection of a causal relation.*
23 *Such evidence...should be...judged as favoring rejection only when a rigorously*

1 performed epidemiologic study (or a meta-analysis of several such studies) of adequate
2 size (i.e., statistical power)...does...not detect a significant association between...WTC
3 exposure...and the adverse event. The absence of demonstrated biologic
4 plausibility...should be...considered supportive of a decision to reject a causal relation
5 but insufficient on its own to shift the balance of evidence from other sources.

6 Level 4: The evidence is inadequate to accept or reject a causal relation: One or
7 more... case reports or epidemiologic studies...are available...but the evidence for a
8 causal relation neither...outweighs...nor...is...outweighed by the evidence against a
9 causal relation. The presence or absence of demonstrated biologic plausibility...should
10 be... considered insufficient to shift this balance in either direction.

11 Level 5: No evidence bearing on a causal relation: Putative associations
12 between...WTC exposures...and adverse events...that are not addressed by...any case
13 reports or epidemiologic studies...should be...placed in this category. Demonstrated
14 biologic plausibility alone...should be...considered insufficient to remove a
15 given...WTC...-adverse event association from this category.

16 As epidemiological information and relevant case reports accumulate, the
17 evidence for or against association of WTC exposures with medical conditions will
18 change, thus possibly changing which of the 5 levels is used to categorize causation of
19 particular adverse health outcomes. It will therefore be of great importance to follow
20 new information and apply it as it becomes available.

21 **Challenges and Recommendations for Application of the Guidelines**

22 There are many challenges to the application of these guidelines. Perhaps the
23 most important challenges are knowledge gaps that cause great uncertainty about

1 evaluation of data and assessment of causation. There is little information from relevant
2 control groups that can be used to generate clear and non-controversial reference values
3 for assessments of mineral particle and mineral fiber levels in the lungs of WTC-exposed
4 individuals. It is unknown at what rate clearance of these materials from the lungs of
5 exposed individuals will occur, further complicating the use of these measurements in
6 assessing exposures.

7 An especially difficult problem is that adequate epidemiological data does not yet
8 exist to quantify relationships between WTC exposures and diseases causing death. This
9 is an important issue for assessment of causation of diseases that occur with appreciable
10 background rates in unexposed people. Examples of WTC-related conditions that are
11 common in both exposed and unexposed populations include upper airway cough
12 syndrome, asthma, and gastrointestinal reflux disease (Brackbill et al. 2006; CDC 2002;
13 Landrigan et al. 2004; Prezant et al. 2002; Skloot et al. 2004). In the absence of uniquely
14 WTC-related pathology, assessing causation by WTC exposures of individual deaths
15 from common conditions will likely continue to be an area of controversy so long as
16 definitive epidemiological findings are unavailable. Should clusters of rare conditions be
17 detected in exposed populations, attributing individual deaths from such conditions to
18 WTC exposures may be less controversial.

19 Another challenge to the use of autopsies in understanding pathologies affecting
20 the exposed population as a whole is that, in general, autopsy rates are very low. Thus,
21 autopsy data will be affected by whatever selection bias is introduced by only evaluating
22 information for those decedents for which there was motivation to obtain autopsies.
23 Autopsy information on a broader group might be obtained if follow-up programs like the

1 Mount Sinai World Trade Center Medical Monitoring Program, the FDNY WTC Medical
2 Monitoring and Treatment Program, and the World Trade Center Health Registry were
3 engaged to explain the scientific and personal value of postmortem examination to their
4 populations in advance of death.

5 The pressures induced by implications of autopsy findings for compensation,
6 litigation, and media scrutiny represent additional challenges to those engaged in post-
7 mortem evaluation of individuals who were exposed to the WTC collapse.

8 The following measures are recommended to address these challenges:

9 1) Research: Research is especially needed to document epidemiologic
10 associations between WTC exposures and disease; and to develop, standardize, and
11 generate guidelines for interpretation of lung mineral particle and mineral fiber burdens.

12 2) Promote autopsies: Measures are needed to promote autopsies for decedents
13 with a history of exposure to the WTC collapse.

14 3) Create a system for storage, inventory tracking, and provision of access to
15 retained tissues and body fluids: An organized approach to sample storage, inventory
16 tracking, and access would facilitate re-evaluation of old samples with new tests; and
17 would be useful for future research investigations. Ideally, this “tissue banking” system
18 would also be able to accommodate biopsy specimens taken as part of diagnostic work-
19 ups on patients, since such specimens could be as, or even more, informative than
20 autopsy specimens.

21 4) Establish an expert panel for initial implementation of the guidelines: This
22 expert panel would be multidisciplinary in membership, including expertise in pathology,
23 clinical evaluation and care of the medical problems of WTC-exposed people, and

1 epidemiology. Clinical expertise represented might include both generalists and
2 specialists in areas such as occupational and environmental medicine, pulmonary
3 medicine, and other specialties as dictated by patterns of disease in WTC-exposed people.
4 Likewise, pathology expertise represented might include both generalists and specialists
5 in pulmonary pathology, toxicology, and other areas relevant to diseases experienced by
6 WTC-exposed people. Although many details would need to be resolved about the
7 nature of the expert panel and its specific policies and procedures, its general missions
8 would include the following:

9 (A) Disseminate and promote use of protocols for a standardized approach to
10 postmortem examination to those in the community engaged in the evaluation of
11 individuals who die, potentially, from exposure to the WTC collapse. The protocols will
12 provide guidance on the use of pathological and other information (such as antemortem
13 clinical data and exposure information) to ascertain, to the extent possible, causation of
14 pathology and death by WTC-related exposures. The expert panel will also review and
15 update protocols at appropriate intervals.

16 (B) Periodically review the scientific literature for epidemiological studies, case
17 reports, and studies demonstrating biological plausibility relevant to assessing causation
18 by WTC-related exposures of diseases causing death. For specific causes of death, the
19 expert panel will designate (and update prior designations, as warranted) levels of
20 evidence indicating potential causation by WTC-related exposures. The expert panel will
21 disseminate their designations to stakeholders and will use them to assign level of
22 causation in individual cases reviewed by the panel (see below).

1 (C) Upon request, review autopsy materials from individual cases referred by
2 stakeholders, including families, physicians, or public health officials. Such reviews
3 would apply standard protocols and designated levels of evidence for causation of various
4 diseases developed by the expert panel (see above) to achieve uniform characterization of
5 pathological abnormalities. Although the expert panel will develop the precise
6 procedures to be followed, it is anticipated that case evaluations will involve review of
7 histology by several pathologists and discussion of pathological, clinical, and
8 mineralogical information by the group. The results of individual autopsy reviews
9 conducted by the expert panel will be reported to requestors, as appropriate, but
10 individually identifiable information will otherwise be kept confidential in compliance
11 with applicable rules and regulations.

12 (D) Coordinate and oversee creation of a secure electronic database of individual
13 cases referred to the expert panel for review of autopsy materials. Information stored in
14 the database will be used to evaluate for patterns in deaths potentially due to WTC
15 exposures. The expert panel will report on its assessments and findings in evaluation of
16 cases to the medical and scientific communities and public at regular intervals. In
17 general, such data will be reported in aggregate form to protect individual confidentiality.

18 (E) Identify research needs. While the expert panel will not have a primary role
19 to conduct research, it will have a unique ability to identify particular causes of death
20 that should be studied to document epidemiologic associations with WTC exposures. It
21 may also be in a position to facilitate collaborations among researchers and clinicians and
22 suggest research materials.

1 **Conclusion**

2 These guidelines have been developed in response to the need for a standardized
3 approach to postmortem examination of individuals exposed to the WTC disaster. This is
4 a need for the entire nation. Postmortem examination in the setting of death after WTC
5 exposure involves integration of pathological, clinical, and exposure information. At the
6 current time, there will often be insufficient epidemiological data or case reports to help
7 definitively determine whether exposures related to the WTC collapse caused death. As
8 additional information becomes available, the nature of these relationships will become
9 more apparent. The autopsy has a key role to play in this process. These guidelines are
10 intended not only to help the families of decedents, but also to provide pathological data
11 to help clinicians better understand and treat conditions affecting survivors of the WTC
12 collapse.

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